Doc Code: AP.PRE.REQ

PTO/SB/33 (07-05)
Approved for use through xx/xx/200x. OMB 0651-00xx
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

PRE-APPEAL BRIEF REQUEST FOR REVIEW	Docket Number (Optional) SY9-155RCE

	Application Number	Filed
	09/745920-Conf. #2871	December 21, 2000
	First Named Inventor: Kenneth C. PARKER	
	Art Unit: 1631	Examiner: Anna Skibinsky

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

- [ ] applicant /inventor.
- [ ] assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)
- [x] attorney or agent of record. Registration number 47,411
- [ ] attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34. _____

Signature

Michael J. Bastian, Ph.D.
Typed or printed name

(617) 227-7400
Telephone number

March 2, 2006
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

- [ ] *Total of 1 forms are submitted.

Express Mail Label No. EV682329110US Dated: March 2, 2006

I hereby certify that this correspondence is being deposited with the U.S. Postal Service as Express Mail, Airbill No. EV682329110US in an envelope addressed to: MS AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date shown below.

Dated: March 2, 2006 Signature: (Michael J. Bastian, Ph.D.)

Docket No.: SY9-155RCE
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Kenneth C. Parker

Application No.: 09/745920 Confirmation No.: 2871

Filed: December 21, 2000 Art Unit: 1631

For: METHODS AND APPARATUS FOR MASS FINGERPRINTING OF BIOMOLECULES Examiner: Anna Skibinsky

PRE-APPEAL BRIEF REQUEST FOR REVIEW

MS AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

INTRODUCTORY COMMENTS

In accordance with the Official Gazette Notice of 12 July 2005, Applicant hereby requests a pre-appeal brief review of the legal and factual basis of the rejections of claims 1-7, 9-24, and 26-29 of the present application prior to the filing of an Appeal Brief.

The present application was originally filed on December 21, 2000, a first Office Action was issued on March 11, 2003, and a response filed thereto on August 1, 2003. A second non-final Office Action was issued on January 12, 2004, and a response thereto filed on June 14, 2004. On October 6, 2004, the response of June 2004 was resubmitted to correct matters of form in response to the Office Communication of September 15, 2004. A final Office Action was issued on December 17, 2004, and a Request for Continued Examination application ("the RCE Application") was filed in response thereto on March 16, 2005.

In the RCE Application, claims 1-7, 9-24, and 26-29 were originally rejected in an Office Action dated April 22, 2005 ("the First Action"). Applicant filed a response to the First Action on July 22, 2005. Applicant's claims were finally rejected in an Office Action dated November 2, 2005 ("the Final Action"). In response to the Final Action, Applicant files concurrently herewith a Notice of Appeal and the present Pre-Appeal Brief Request for Review.

An extension of time to respond to the Final Action is requested, and a Petition for said extension is filed concurrently herewith. Applicant believes that no additional fees are due with

this Request; if this belief is in error the Director is hereby authorized to charge any required fee to Deposit Account No. 12-0080, under Order No. SY9-155RCE.

REMARKS

Claims 1-7, 9-24, and 26-29 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over U.S. Patent No. 6,017,693 ("Yates") in view of U.S. Patent No. 5,710,213 ("Wright") and the article "*Improving protein identification from peptide mass fingerprinting through a parameterized multi-level scoring algorithm and optimized peak detection*" in Electrophoresis 1999, Volume 20, pages 3535-3550 by Gras, et al. ("Gras") (collectively "the cited references").

Applicant notes that although Wright is cited as a basis for the rejections, the Final Action points to no portion of Wright as teaching or suggesting any portion of Applicant's claims or the combination of Yates and Gras. Accordingly, Applicant believes that the Wright reference does not form a part of the rejections currently being applied.

Applicant submits that the cited references, either alone or in combination, fail to teach or suggest all elements of Applicant's claims, or these claims as a whole. The cited references do not teach or suggest "determining a biomolecule fragment score" of a mass signal using, *inter alia*, a mass signal intensity, a biomolecule fragment detection parameter, and a mass error for the mass signal, as set forth in Applicant's claims. Accordingly, Applicant submits the Final Office Action fails to establish a *prima facie* case of obviousness against the pending claims.

Specifically, Applicant's independent claims 1 and 23, each require a step of:

> determining a biomolecule fragment score for said mass signal, wherein said biomolecule fragment score comprises a function of:
>
> the mass signal intensity for said mass signal,
>
> a biomolecule fragment detection parameter for a biomolecule fragment of said potential source biomolecule, said biological fragment detection parameter for said biomolecule fragment comprises a numerical value that is a measure of the likelihood of detecting the biomolecule fragment as a fragment, digestion product, or both, of said potential source biomolecule, the likelihood of detecting said biological fragment being based at least in part on relative mass signal intensity relationships between biomolecule fragments, fractions of biomolecule fragments, or both; and
>
> a mass error for said mass signal from the relative difference between a mass which corresponds to said mass signal and a mass of the biomolecule fragment;

(emphasis added). Applicant submits that the Final Office Action has failed to show how the cited references teach or suggest, either alone or in combination, the above quoted determining step or the claims as a whole. In particular, the Final Office Action has failed to show where the cited references teach or suggest a "biomolecule fragment detection parameter" as that term is used in the claims.

Applicant has previously described the term "biomolecule fragment detection parameter" on the record in the response of August 1, 2003, for example at page 27, line 9, to page 29, line 2, and asks the panel to refer to these descriptions.

Applicant reads the Final Action as stating (pages 2-3) that the element of a "biomolecule fragment detection parameter" is not found in Yates but rather in Gras. Applicant agrees that Yates does not teach or suggest using mass signal intensity to determine either a "biomolecule fragment score" or a "biological fragment detection parameter" as set forth in the claims.

Applicant, however, disagrees with the position that Gras teaches or suggests a "biomolecule fragment score" that is a function of a "biological fragment detection parameter" as set forth in Applicant's claims. The Final Action states at page 3 (emphasis added):

> Gras et al teaches the calculation of an "identification score"...and defines the parameters for the scoring function in Section 2.4.3.2...This was pointed to on page 6, lines 11-13 in the Office Action of April 22, 2005....The limitation in claim 1 recites that a biomolecule fragment score comprises a function of a biomolecule fragment detection parameter which is the "likelihood of detecting said biomolecule fragment...based at least in part on relative mass signal intensity relationships." Gras et al. also uses, in part, the intensity of peaks to determine a score for matching searched protein and candidate proteins through peptide mass fingerprinting.

The Final Action, however, fails to show how Gras's use of peak intensity to determine a score provides, teaches or suggests "the likelihood of detecting said biological fragment being based at least in part on relative mass signal intensity relationships between biomolecule fragments, fractions of biomolecule fragments, or both" for a biomolecule fragment. Rather, for a given mass signal (peak), Gras only uses the intensity of that peak in his "score" for that peak.

Specifically, in the terminology of Gras, at the "mass level" or "level 1" (see, e.g., Gras at page 3542, section 2.4.3.2) for a given peak (e.g., peptide mass) Gras uses only "the intensity of the corresponding peak in the mass spectrum," $coef_i(a)$, to calculate a score at this level. Gras does not teach or suggest using relative mass signal intensity relationships in calculating a score for a given biomolecule fragment such as a peptide. As a result, the Final Action's assertion that

Gras' use of signal intensity teaches use of relative mass signal intensity relationships as set forth in the clams is a clear error. Accordingly, the Final Action does not establish that the element of a "biomolecule fragment detection parameter" as used in the claims is taught by the cited references, either alone or in combination.

Gras' use of such parameters as number of chemical modifications, and number of missed cleavages and their associated coefficients also do not provide a "biomolecule fragment detection parameter" based at least in part on relative mass signal intensity relationships as set forth in Applicant's claims, and Applicant does not believe the Final Action asserts otherwise. Nevertheless, Applicant notes that Gras uses the parameters of number of chemical modifications, and number of missed cleavages to determine the confidence of a match:

> At the mass level, the first goal is to determine the quality of a peak, that is to determine when a peak may be considered a "true" peak. For that purpose...[a] level of confidence is also defined for the match of an experimental mass with a theoretical mass...with the help of parameters such as the number of modifications, the number of missed cleavages necessary for the match...

(Gras at page 3541, 2nd column, last paragraph). Accordingly, Gras teaches and uses the chemical modifications and missed cleavages parameters as a measure of matching tolerance based on mass.

In the field of mass spectrometric analysis, mass difference is distinctly different from and not equatable with the signal intensity associated with a mass signal. A glance at a typical mass spectrum with the x-axis representing mass and the y-axis representing intensity shows that intensity and mass are two distinct physical quantities. A comparison of the physical units associated with mass (e.g., kg) and intensity (ultimately related to current, e.g. amp, as detection is typically done electronically) shows that mass cannot reasonably be interpreted as intensity or its equivalent. As a result, mass error, matching or confidence levels based on mass differences do not take into account the likelihood of detecting a peptide as a mass signal in the mass spectrum of a sample containing that peptide or reflect general relative mass signal intensity relationships. Accordingly, the parameters of number of chemical modifications and number of missed cleavages as taught by Gras cannot be interpreted as a "biomolecule fragment detection parameter" as this term is used in Applicant's claims.

Applicant does not understand the statements in the Final Action at pages 3-4 with respect to "mass level...which corresponds to the mass error" or the "level 2" or protein level

parameters of Gras that "include the confidence level for the match" based on comparing experimental and theoretical masses of the protein, to assert that either one of these can be equated to a "biological fragment detection parameter" as set forth in Applicant's claims for determining a "biomolecule fragment score"; but to the extent such may be asserted, Applicant must disagree for the reasons set forth above that mass difference or confidence level parameters based on mass, as taught in the cited references, cannot be interpreted as a "biomolecule fragment detection parameter" to determine a "biomolecule fragment score" as those terms are used in Applicant's claims.

For the reasons stated above, Applicant does not believe Wright forms a basis for the present rejections. Nevertheless, Applicant submits that Wright, either alone or in combination with Gras and/or Yates, does not provide the teachings missing in Yates and Gras of a "biomolecule fragment detection parameter" as set forth in Applicant's claims.

CONCLUSION

The "determining a biomolecule fragment score" step is a specific step of Applicant's method claims that must be taught by the cited references to render Applicant's claims obvious. The "biomolecule fragment score" of a mass signal is further limited as being determined from, *inter alia*, a biomolecule fragment detection parameter for said mass signal based, at least in part, on relative mass signal intensity relationships between biomolecule fragments (and/or fractions thereof). Accordingly, as the Final Action has failed to show where the cited references teach or suggest determining a biomolecule fragment detection parameter using at least in part relative mass signal intensity relationships, Applicant submits that the Final Action has failed to establish a *prima facie* case of obviousness against Applicant's claims. In view of the above, it is believed that all presently pending claims are in condition for allowance, and it is respectfully requested that the application be passed to issue.

Dated: March 2, 2006

Respectfully submitted,

By _____
Michael J. Bastian, Ph.D.
Registration No.: 47,411

Attorney/Agent For Applicant

LAHIVE & COCKFIELD, LLP
28 State Street
Boston, Massachusetts 02109
(617) 227-7400; (617) 742-4214 (Fax)